

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Parts 310 and 358

[Docket No. 2005N-0448]

RIN 0910-AF49

**Dandruff, Seborrheic Dermatitis, and Psoriasis Drug Products Containing Coal Tar and Menthol for Over-the-Counter Human Use; Proposed Amendment to the Monograph**

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Proposed rule.

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**SUMMARY:** The Food and Drug Administration (FDA) is issuing a proposed rule to amend the final monograph (FM) for over-the-counter (OTC) dandruff, seborrheic dermatitis, and psoriasis drug products to include the combination of 1.8 percent coal tar solution and 1.5 percent menthol in a shampoo drug product to control dandruff. FDA is issuing this proposed rule after considering information submitted in a citizen petition. This proposal is part of FDA's ongoing review of OTC drug products.

**DATES:** Submit written or electronic comments by *[insert date 90 days after date of publication in the Federal Register]*. See section IX of this document for the proposed effective date of any final rule that may publish based on this proposal.

**ADDRESSES:** You may submit comments, identified by Docket No. 2005N-0448 and RIN 0910-AF49, by any of the following methods:

*Electronic Submissions*

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2005N-0448

NPR 1

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Certifier	L. CLAWSON
DDM	

Submit electronic comments in the following ways:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.
- Agency Web site: <http://www.fda.gov/dockets/ecomments>. Follow the instructions for submitting comments on the agency Web site.

### *Written Submissions*

Submit written submissions in the following ways:

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier [For paper, disk, or CD-ROM submissions]:  
Division of Dockets Management (HFA-305), Food and Drug Administration,  
5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal or the agency Web site, as described in the *Electronic Submissions* portion of this paragraph.

*Instructions:* All submissions received must include the agency name and Docket No. 2005N-0448. All comments received may be posted without change to <http://www.fda.gov/ohrms/dockets/default.htm>, including any personal information provided. For additional information on submitting comments, see the “Comments” heading of the **SUPPLEMENTARY INFORMATION** section of this document.

*Docket:* For access to the docket to read background documents or comments received, go to <http://www.fda.gov/dockets/default.htm> and insert the docket number, found in brackets in the heading of this document, into

the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

**FOR FURTHER INFORMATION CONTACT:** Michael L. Koenig, Center for Drug Evaluation and Research (HFD-560), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-827-2222.

**SUPPLEMENTARY INFORMATION:**

**I. Background**

In the **Federal Register** of December 4, 1979 (44 FR 69768), FDA published an advance notice of proposed rulemaking (ANPR) to establish a monograph for OTC external analgesic drug products. The ANPR includes the recommendations of the Advisory Review Panel on OTC Topical Analgesic, Antirheumatic, Otic, Burn, and Sunburn Prevention and Treatment Drug Products (the Topical Analgesic Panel). The Topical Analgesic Panel concluded that menthol is safe and effective for use as an OTC external antipruritic (anti-itch) ingredient in concentrations of 1.0 percent or less and as a topical counterirritant in concentrations exceeding 1.25 percent up to 16 percent. In the **Federal Register** of February 8, 1983 (48 FR 5852), FDA’s proposed monograph, or tentative final monograph (TFM), for OTC external analgesic drug products included menthol as an antipruritic ingredient at concentrations from 0.1 percent to 1.0 percent.

In the **Federal Register** of December 3, 1982 (47 FR 54646), FDA published an ANPR to establish a monograph for OTC dandruff, seborrheic dermatitis, and psoriasis drug products. The ANPR includes the recommendations of the Advisory Review Panel on OTC Miscellaneous External Drug Products (the Miscellaneous External Panel) concerning OTC drug products for the control of dandruff, seborrheic dermatitis, and psoriasis. The Miscellaneous External

Panel recommended coal tar preparations as safe and effective for use as shampoos for controlling dandruff. The Miscellaneous External Panel also concluded that menthol is safe at concentrations of 0.04 to 1.5 percent, but that there were insufficient effectiveness data to include it in the monograph for controlling dandruff. The Miscellaneous External Panel further noted that the temporary relief of itching does not amount to control of dandruff.

In the **Federal Register** of July 30, 1986 (51 FR 27346), FDA published its TFM for OTC dandruff, seborrheic dermatitis, and psoriasis drug products. No new information was submitted for menthol. Therefore, menthol was not included in the TFM.

In the **Federal Register** of December 4, 1991 (56 FR 63554), FDA issued an FM for OTC dandruff, seborrheic dermatitis, and psoriasis drug products in part 358, subpart H (21 CFR part 358, subpart H). The FM included discussion of a study comparing a shampoo product containing the combination of 9 percent coal tar solution and 1.5 percent menthol versus a shampoo containing only the coal tar for relieving scalp itching associated with dandruff (Ref. 1). FDA determined that the study had a number of major flaws and did not demonstrate that the combination product offers any advantage over the product containing only coal tar (56 FR 63554 at 63562 to 63564). Therefore, FDA concluded that the coal tar-menthol combination is not generally recognized as safe and effective (GRASE) for the control of dandruff and placed this combination in a list of active ingredients found not to be GRASE (21 CFR 310.545(d)(3)).

## **II. FDA's Tentative Conclusions on the Petition**

In 1993, FDA received a petition (Ref. 2) to amend the FM for OTC dandruff, seborrheic dermatitis, and psoriasis drug products to include the

combination of 9 percent coal tar solution and 1.5 percent menthol in a shampoo drug product to relieve scalp itching associated with dandruff. The petitioner subsequently clarified that the coal tar concentration of 9 percent was actually 9 percent, on a volume-to-volume basis, of a 20 percent coal tar solution, on a weight-to-volume basis. Thus, the final concentration of the coal tar solution used in the study was 1.8 percent on a weight-to-volume basis (Ref. 3). The petition includes results of a three-arm clinical study evaluating the effectiveness of the ingredients in combination compared to 1.8 percent coal tar alone and 1.5 percent menthol alone. Both menthol alone and the combination of coal tar and menthol provided additional itch relief at 5, 15, and 30 minutes over coal tar alone, and the difference in itch relief was statistically significant ( $p \leq 0.05$ ). The study did not examine relief of scaling (i.e., control of dandruff). FDA tentatively concludes that this study supports the combination of 1.8 percent coal tar solution and 1.5 percent menthol in a shampoo to provide more or additional relief of itching associated with dandruff over 1.8 percent coal tar alone. FDA's detailed comments and evaluation of the study are on file in the Division of Dockets Management (Ref. 4).

### **III. FDA's Proposal**

Based on the study submitted in the petition and FDA's previous conclusion that coal tar is GRASE for the control of dandruff, FDA believes the combination of 1.8 percent coal tar and 1.5 percent menthol in a shampoo is GRASE to control dandruff and relieve itching associated with dandruff. FDA proposes to include this new combination in § 358.720 and remove the combination from § 310.545(d)(3). Because data on a range of concentrations for coal tar and menthol have not been submitted, FDA is proposing to amend

the FM to include only the concentration of each active ingredient used in the study. Although the 1.5 percent concentration for menthol exceeds the 1.0 percent maximum currently proposed for the ingredient as an antipruritic (see proposed § 348.10(b)(6), 48 FR 5852 at 5867), this use of menthol is different, because the product will be applied to hair that has been thoroughly wetted and subsequently rinsed. Furthermore, the menthol is likely diluted to below 1.0 percent concentration immediately. FDA is not proposing menthol as a single active ingredient for the control or relief of symptoms of dandruff because FDA has not received any data demonstrating that menthol alone is GRASE for this indication.

FDA is proposing that labeling for this combination in proposed § 358.760 be as follows:

- Statement of identity: “dandruff/anti-itch shampoo” or “antidandruff/anti-itch shampoo” (proposed § 358.760(a)(1))
- Indication: “[bullet] [select one of the following: ‘for relief of’ or ‘controls’] the symptoms of dandruff [bullet] [select one of the following: ‘additional’ or ‘extra’] relief of itching due to dandruff” (proposed § 358.760(b)(1) and (b)(2))
- Warnings: those listed in § 358.750(c)(1) and (c)(2) (proposed § 358.760(c))
- Directions: “[bullet] wet hair [bullet] apply shampoo and work into a lather [bullet] rinse thoroughly [bullet] for best results, use at least twice a week or as directed by a doctor” (proposed § 358.760(d)(1))

FDA believes the proposed labeling for coal tar-menthol combination drug products reflects the scientific data, which demonstrate the combination provides additional itch relief over coal tar alone. FDA proposes a statement

of identity for this product that reflects the antidandruff action of coal tar as well as the anti-itch action of menthol. When comparing coal tar products labeled as “dandruff shampoo” with combination coal tar-menthol products labeled as “dandruff/anti-itch shampoo,” consumers will be informed that the combination products contain menthol for more itch relief than provided by coal tar alone.

FDA also proposes to include this additional anti-itch action under the “Uses” heading in the Drug Facts labeling. FDA is proposing a similar indication statement for coal tar-menthol combination products as that included in the dandruff monograph for other coal tar products (§ 358.750(b)). In addition, FDA proposes a second indication statement for coal tar-menthol combination products only: “[bullet] [select one of the following: ‘additional’ or ‘extra’] relief of itching due to dandruff”. This indication reflects the data from the submitted study (Ref. 2) by informing consumers that the combination product provides more itch relief than coal tar alone.

Because the warnings for menthol in the proposed rule for OTC external analgesic drug products (48 FR 5852 at 5868) are similar to those for coal tar in the dandruff monograph (§ 358.750(c)(1) and (c)(2)), FDA proposes the same warnings for the combination as for coal tar alone. The directions proposed for the combination product specify that the product be a shampoo applied to wetted hair and thoroughly removed from the scalp after brief exposure. FDA is not proposing to include formulations that are applied and left on the skin or scalp (e.g., creams, ointments, lotions, or hairgrooms) because FDA has only reviewed safety and effectiveness data for coal tar-menthol combination drug products in a shampoo.

#### IV. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601–612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104–4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). Under the Regulatory Flexibility Act, if a rule may have a significant economic impact on a substantial number of small entities, an agency must analyze regulatory options that would minimize any significant impact of the rule on small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of costs and benefits, before proposing “any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100 million or more (adjusted annually for inflation) in any one year.”

FDA tentatively concludes that this proposed rule is consistent with the principles set out in Executive Order 12866 and in these two statutes. This proposed rule is not a significant regulatory action as defined by the Executive order and so is not subject to review under the Executive order. As discussed in this section of the document, FDA has tentatively determined that this proposed rule will not have significant economic impact on a substantial number of small entities under the Regulatory Flexibility Act. The Unfunded Mandates Reform Act does not require FDA to prepare a statement of costs



and benefits for this proposed rule because the proposed rule is not expected to result in any 1-year expenditure that would meet or exceed \$100 million adjusted for inflation. The current threshold after adjustment for inflation is about \$115 million, using the most current (2003) Implicit Price Deflator for the Gross Domestic Product.

The purpose of this proposed rule is to allow an additional combination of active ingredients for OTC antidandruff drug products. Manufacturers can reformulate their OTC antidandruff drug products that contain coal tar to include the combination or can manufacture a new combination product containing coal tar and menthol. Reformulating or manufacturing a new combination product might result in additional product sales but, in either case, is completely optional. Thus, this proposed rule will not impose a significant economic burden on affected entities. Therefore, FDA certifies that this proposed rule will not have a significant economic impact on a substantial number of small entities. No further analysis is required under the Regulatory Flexibility Act (5 U.S.C. 605(b)).

FDA invites public comment regarding any substantial or significant economic impact that this proposed rule would have on manufacturers of OTC drug products for the control of dandruff. Types of impact may include, but are not limited to, costs associated with manufacturing, labeling, or repackaging. Comments regarding the impact of this proposed rule should be accompanied by appropriate documentation. FDA is providing a period of 90 days, from the date of publication of this proposed rule in the **Federal Register**, to develop and submit comments on this subject. FDA will evaluate any comments and supporting data that are received and will reassess the economic impact of this proposed rule in the preamble to the final rule.

## **V. Paperwork Reduction Act of 1995**

FDA tentatively concludes that the labeling requirements proposed in this document are not subject to review by the Office of Management and Budget because they do not constitute a “collection of information” under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 *et seq.*). Rather, the proposed labeling statements are a “public disclosure of information originally supplied by the Federal Government to the recipient for the purpose of disclosure to the public” (5 CFR 1320.3(c)(2)).

## **VI. Environmental Impact**

FDA has determined under 21 CFR 25.31(a) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

## **VII. Federalism**

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the proposed rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, FDA tentatively concludes that the proposed rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement has not been prepared.

## **VIII. Request for Comment**

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this proposal and on FDA’s economic impact determination. Submit a single copy of electronic

comments or two paper copies of any mailed comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

#### **IX. Proposed Effective Date**

FDA is proposing that any final rule that may issue based on this proposal become effective 30 days after its date of publication in the **Federal Register**.

#### **X. References**

The following references are on display in the Division of Dockets Management (see **ADDRESSES**) under Docket No. 1982N-0214 and may be seen by interested persons between 9 a.m. and 4 p.m., Monday through Friday.

1. Comment No. RPT.
2. Comment No. PR 1.
3. Comment No. LET 13.
4. Comment No. LET 14.

#### **List of Subjects**

##### *21 CFR Part 310*

Administrative practice and procedure, Drugs, Labeling, Medical devices, Reporting and recordkeeping requirements.

##### *21 CFR Part 358*

Labeling, Over-the-counter drugs.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR parts 310 and 358 be amended as follows:

## PART 310—NEW DRUGS

1. The authority citation for 21 CFR part 310 continues to read as follows:

**Authority:** 21 U.S.C. 321, 331, 351, 352, 353, 355, 360b–360f, 360j, 361(a), 371, 374, 375, 379e; 42 U.S.C. 216, 241, 242(a), 262, 263b–263n.

2. Section 310.545 is amended by revising paragraph (d)(3) to read as follows:

**§ 310.545 Drug products containing certain active ingredients offered over-the-counter (OTC) for certain uses.**

\* \* \* \* \*

(d) \* \* \*

(3) December 4, 1992, for products subject to paragraph (a)(7) of this section that contain menthol as an antipruritic in combination with the antidandruff ingredient coal tar identified in § 358.710(a)(1) of this chapter. This section does not apply to products allowed by § 358.720(b) of this chapter after [date 30 days after date of publication of a final rule in the **Federal Register**].

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## PART 358—MISCELLANEOUS EXTERNAL DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

3. The authority citation for 21 CFR part 358 continues to read as follows:

**Authority:** 21 U.S.C. 321, 351, 352, 353, 355, 360, 371.

4. Section 358.720 is revised to read as follows:

**§ 358.720 Permitted combinations of active ingredients.**

(a) *Combination of active ingredients for the control of dandruff.* Salicylic acid identified in § 358.710(a)(4) may be combined with sulfur identified in

§ 358.710(a)(6) provided each ingredient is present within the established concentration and the product is labeled according to § 358.750.

(b) *Combination of control of dandruff and external analgesic active ingredients.* Coal tar identified in § 358.710(a)(1) may be used at a concentration of 1.8 percent coal tar solution, on a weight-to-volume basis, in combination with menthol, 1.5 percent, in a shampoo formulation provided the product is labeled according to § 358.760.

5. New § 358.760 is added to subpart H to read as follows:

**§ 358.760      Labeling of permitted combinations of active ingredients for the control of dandruff.**

The statement of identity, indications, warnings, and directions for use, respectively, applicable to each ingredient in the product may be combined to eliminate duplicative words or phrases so that the resulting information is clear and understandable.

(a) *Statement of identity.* For a combination drug product that has an established name, the labeling of the product states the established name of the combination drug product, followed by the statement of identity for each ingredient in the combination, as established in the statement of identity sections of the applicable OTC drug monographs.

(1) *Combinations of control of dandruff and external analgesic active ingredients in § 358.720(b).* The label states “dandruff/anti-itch shampoo” or “antidandruff/anti-itch shampoo”.

(2) [Reserved]

(b) *Indications.* The labeling of the product states, under the heading “Uses,” one or more of the phrases listed in this paragraph (b), as appropriate. Other truthful and nonmisleading statements, describing only the uses that have been established and listed in this paragraph (b), may also be used, as

provided in § 330.1(c)(2) of this chapter, subject to the provisions of section 502 of the Federal Food, Drug, and Cosmetic Act (the act) relating to misbranding and the prohibition in section 301(d) of the act against the introduction or delivery for introduction into interstate commerce of unapproved new drugs in violation of section 505(a) of the act.

(1) *Combinations of control of dandruff and external analgesic active ingredients in § 358.720(b).* The labeling states “[bullet] [select one of the following: ‘for relief of’ or ‘controls’] the symptoms of dandruff [bullet] [select one of the following: ‘additional’ or ‘extra’] relief of itching due to dandruff”.

(2) The following terms or phrases may be used in place of or in addition to the words “for relief of” or “controls” in the indications in paragraph (b)(1) of this section: “fights,” “reduces,” “helps eliminate,” “helps stop,” “controls recurrence of,” “fights recurrence of,” “helps prevent recurrence of,” “reduces recurrence of,” “helps eliminate recurrence of,” “helps stop recurrence of”.

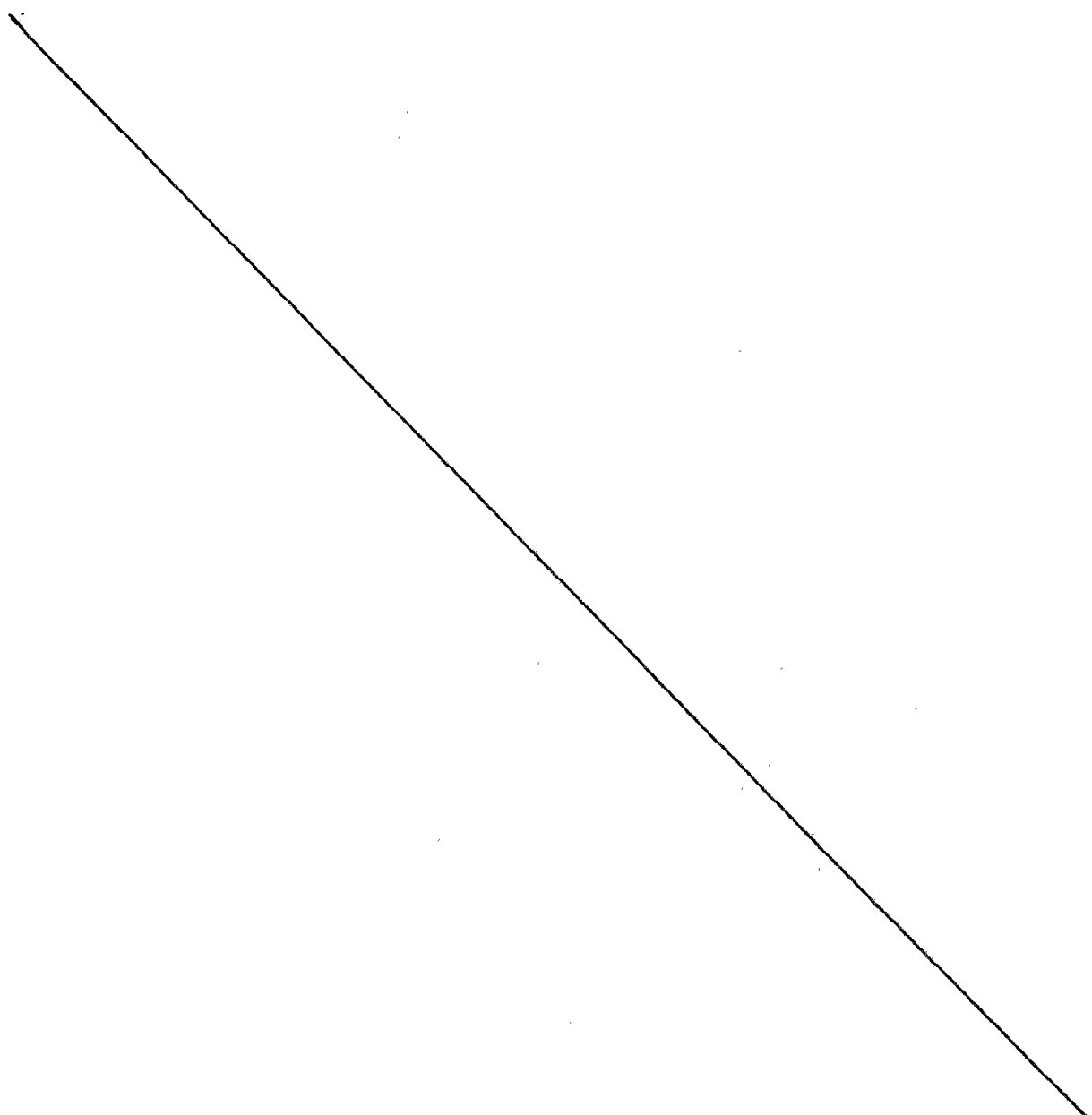
(3) The following terms may be used in place of the words “the symptoms of” in the indication in paragraph (b)(1) of this section: “scalp” (select one or more of the following: “itching,” “irritation,” “redness,” “flaking,” “scaling”) “associated with”.

(c) *Warnings.* The labeling of the product states, under the heading “Warnings,” the warning(s) listed in § 358.750(c)(1) and (c)(2).

(d) *Directions.* The labeling of the product states, under the heading “Directions,” directions that conform to the directions established for each ingredient in the directions sections of the applicable OTC drug monographs, unless otherwise stated in this paragraph (d). When the time intervals or age limitations for administration of the individual ingredients differ, the directions for the combination product may not contain any dosage that

exceeds those established for any individual ingredient in the applicable OTC drug monograph(s), and may not provide for use by any age group lower than the highest minimum age limit established for any individual ingredient.

(1) *Combinations of control of dandruff and external analgesic active ingredients in § 358.720(b).* The labeling states “[bullet] wet hair [bullet] apply shampoo and work into a lather [bullet] rinse thoroughly [bullet] for best results, use at least twice a week or as directed by a doctor”.



(2) [Reserved]

Dated: 12/5/05  
December 5, 2005.

  
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Jeffrey Shuren,  
Assistant Commissioner for Policy.

[FR Doc. 05-????? Filed ??-??-05; 8:45 am]

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